

ALL ABOUT MALARIA

Causes • Prevention • Cure

मलरिया

Dr O P Jaggi, M D Ph D

FCCP (USA) FACA (USA) FRAS (London)



ORIENT PAPERBACKS

All About Malaria

© Dr O P Jaggi 1978

**Published by
Orient Paperbacks
(A Division of Vision Books Pvt Ltd)
36-C Connaught Place New Delhi 110001**

**Printed at
Kay Kay Printers
150-D Kamla Nagar Delhi 110007**

Preface

After a lapse of more than two decades malaria has reappeared over large parts of India. More and more cases of the disease are being reported. The whole situation causes concern because the means available to check the spread of malaria are proving less and less useful.

In the situation in which we are today, it is necessary to know the basic facts about malaria: how it is caused, how it is diagnosed, how it is treated, and the most important of all, how to protect oneself from getting it.

This book is intended to inform you about these and other aspects of malaria so that you can protect yourself and others from this disease.

By no means is it intended that by reading it you can do away with the advice of a competent doctor in case it is necessary.

CONTENTS

Preface

1 The Mosquito	9
2 The Malaria Parasite	22
3 Symptoms of Malaria	32
4 Pathological Changes in the Body	42
5 Diagnosis of Malaria	46
6 Anti Malarial Drugs	55
7 Treatment of Malaria Attack	62
8 Treatment of Cerebral Malaria	66
9 Drug Prophylaxis or Suppression of Malaria Attack	70
10 Malaria Immunity and Vaccination	73
11 Prevention of Malaria	78
12 Problems in Malaria Control	89
13 Researches in Malaria Past and Present	96
14 What Can You Do to Prevent Malaria	102

1

The Mosquito

The mosquitoes that we encounter in our surroundings belong to different species. There are about 2700 species of mosquitoes known all over the world. Many of these species act as carriers of different diseases. The four important groups of mosquitoes in India that cause diseases in man are the *Culex*, *Aedes*, *Mansonia* and *Anopheles*.

Malaria is caused in man only by the *Anopheles* species of mosquitoes. Forty five species of *Anopheles* mosquitoes have been identified in India. The species of *Anopheles* that carry malaria are six of these the most prevalent ones are *A. culicifacies* pre-

dominantly present in the rural areas and A stephensi predominantly present in the urban areas

In order to understand how anopheles mosquitoes carry malaria to man and how this propagation of disease can be checked it is necessary that we get familiar with how the mosquito breeds through what stages of growth it passes what are its habits and also its anatomical structure

You might have seen that when you change flowers in a flower vase after some days or when you do not use your air cooler for some days you find in the water moving objects of different sizes and shapes some long and cylindrical moving fast from the surface to the depths others stout and stumpy which tumble down in water when disturbed These are the different stages in the development of mosquitoes which you unintentionally harbour in your own house and which when they become adults are the source of nuisance and disease first for you and then for your neighbours

In order to become adult insect the mosquito passes through four stages of growth (1) the egg (2) the larva (3) the pupa and (4) the adult Let us have a look at the characteristic features of each of these stages in an anopheles mosquito

The Egg

Anopheles eggs are deposited singly too small to

be seen with the naked eye Under the microscope they resemble tiny boats broadest at the middle with the ends somewhat pointed and the upper margins frilled In the mid portion on either side are structures which keep the egg afloat The eggs have a tendency to cluster together with the ends in contact, forming triangular polygonal or stellate patterns on the surface of the water



Anopheles Egg

A mosquito egg is entirely passive It takes no food has no power to move and survives or perishes depending upon the environments Most eggs hatch within 48 hours of laying Moisture and temperature

between 18-25°C tend to increase the survival of the eggs

The Larva

It is a free swimming creature. This is the one you see occasionally swimming about in the water in the flower vase. It has an elongated body divisible



Anopheles Larva

into head, thorax and abdomen. It passes through four stages of growth with moulting between each

stage Anopheles larva floats horizontally in water and has no siphon tube at the tip of its abdomen. The whole larval stage occupies 5 to 7 days.

Different environmental factors influence the development and behaviour of larvae in their breeding places. The more important ones are the presence of other vegetable and animal life, water movement and temperature, sunlight and shade, chemical composition of water, its turbidity and contaminants. Anopheles larvae are more frequently found in association with some types of water plants. Some anopheles grow in tree holes and under fallen leaves.

Some varieties of fish, such as guppy and gambusia, eat up mosquito larvae. In fact, they have been extensively used in some parts of India so as to check the number of mosquitoes.

Larvae are vulnerable to wave action on water. Constant agitation by wind, man or beast may keep a potential breeding place free from larvae. The flush tanks on top of the houses in the cities, if they are working properly and frequently, do not usually allow the mosquitoes to flourish there; if they don't, the mosquitoes breed in them. Shady, though not completely dark places in water, encourage the growth of larvae. Anopheles larvae do not like very low temperatures.

Since anopheles larvae are generally found in clean water in the villages, if you ask a villager where he gets his drinking water, there you

would find the breeding place of local malaria causing mosquito. Clean water, however, is not absolutely essential for anopheles growth.

Anopheles larvae spend most of their time on surface. They appear to ingest anything that comes their way. The bulk of larval food consists of algae and other small animal and vegetable life.

The Pupa

It is a grotesque comma shaped structure in appearance quite unlike larva. It has a large rounded struc-



Anopheles
Pupa

ture which represents head and thorax and a narrow

abdomen Two small respiratory tubes or trumpets project from the upper surface of the thorax The eyes wings legs and antennae of the adult mosquito are all more or less visible through the somewhat transparent covering layer At the end of the abdomen are the two tail fins or paddles by means of which the pupa is able to swim downward through the water in a peculiar tumbling fashion

The pupa takes no food But it swims with considerable agility It normally floats on the surface of water Sudden disturbance even vibrations send it tumbling down to the depths of the water As the pupa reaches maturity it becomes more susceptible to any disturbance Any activity around a breeding place interferes with the emergence of adults and causes high mortality

The Adult

When the development is complete the skin of pupa splits along the back and the adult mosquito emerges The process is completed in two to three minutes but the mosquito remains resting on the pupal skin case for several hours before attempting to fly During this time the natural colours of the species become fixed and the outer covering becomes relatively hard and dry

Under favourable conditions of temperature and



Anopheles Adult

food supply the life cycle from the egg to the adult is completed in 7 to 10 days

Behaviour Characters of Adult Mosquito

Following emergence from the pupal case the anopheles mosquitoes usually resort to sheltered resting places where they remain inactive for some time. Relatively dark places free from wind, not too dry, are the most preferred ones. The first resting places are in close proximity to breeding places and here both sexes are found in equal numbers. Within

the house the mosquitoes often rest in dark corners and lower portions of the walls. In villages cattle sheds are the preferred places both by day and night.

The first flight of a mosquito from a breeding area to a suitable resting place is usually very short. Thereafter the mosquitoes both male and female fly considerable distances. They can cover a distance of up to two miles in about two hours.

The male proboscis is not adapted for piercing so that it feeds only on flower nectar, plant juice and water.

Only the female mosquitoes bite. Some species of mosquitoes that attack man, announce their intention by an annoying hum. They cause pain at the moment of bite and give rise to subsequent itching and swelling. No such crude act is indulged in by anophelines. A majority of the female anophelines mosquitoes make a silent approach and their bite is hardly detected.

Increased humidity and wet perspiring skin attract the mosquitoes for biting. The peculiar odour of the human skin seems to attract them.

Mosquitoes suck at a time blood even larger than their own weight. A 2 mg mosquito after sucking blood may weigh even up to 5 mg.

Biting activity of anophelines mosquitoes is maximum between 10 p.m. and 2 a.m. The young and little older mosquitoes have more or less equal biting

ability A blood meal on the first day of the life of the mosquito is said to increase its longevity

The mosquitoes produce sounds while flying This sound is produced essentially by the rapid movement of the wings and changes in the outline of the thorax due to action of the wing muscles These sounds have significance inasmuch as swarming mating and mass migration are believed to depend upon auditory communication between individual males and females It has been suggested that artificial imitation of such sounds in connection with the operation of mosquito traps might serve as a possible control measure by luring larger numbers to their death The voices of the females are said to be deeper in pitch The voice of a single female can cause males of the same species to burst into a chorus The males orient themselves by turning either the antennae or genitalia in the direction of the source

Why do mosquitoes swarm over your head in the evening when you are outdoors moving along with you as you move? Swarming of the males occurs as a preliminary to the mating act The swarms tend to hover over some tall object such as a tree shrub building or a moving object Females invade the swarm momentarily emerging almost at once united with a male Pairing in *A. stephensi*, a common anopheles usually takes place end to end though there are many variations of position Mating pairs may remain in flight for a short while perhaps

until they encounter some surface on which they may come to rest. More commonly however the two fall to the ground where they may rotate like a whirling ball before separating and then flying away

One mating is usually regarded as sufficient for the functional life of the female though in some species there may be repetition of the mating act.

Anopheles lay their eggs on the surface of the water. This occurs normally at night or in some species just before sunrise. In many species the female rests either on the surface film or on a bit of floating debris, and proceeds to extrude the eggs one at a time upto a total of 100 to 350. The eggs soon float apart and assume interesting geometric shapes. Before laying eggs in some species, the female makes a hovering dance close to the surface of water. A blood meal is usually necessary for the production of viable eggs.

Male mosquitoes have a shorter life-span as compared to the females. Temperature and humidity greatly influence the life span. In hot summer anopheles have been seen to die in two days. Both high and low temperatures are fatal. The usual life span of mosquitoes varies from 10 to 30 days.

Anatomical Structure of the Mosquito

The body of an adult mosquito consists of three ~

The Malaria Parasite

Only a female mosquito
 after bitten a man
 to pass on the
 whom it bites
 malaria patient
 which are
 sites in the
 grow inside
 they have
 changed into
 they capable
 The mosquito

which has
 a post-

a

function in the causation of malaria by (1) letting the malarial parasite grow in its body and (2) passing it on to another person. The real culprit is the malaria parasite.

Let us get familiar with the parasites of malaria so that by recognising them and their potentialities we can take suitable steps in either not getting the disease or having once got it take measures to get rid of them from the body.

The number of known species of malaria parasite in man and animals is around 120. Only four species occur in man. These are (1) *P. vivax*, (2) *P. falciparum*, (3) *P. malariae* and (4) *P. ovale*. Of these *P. vivax* has the widest distribution.

In India, 65 to 69 per cent of malaria fevers are reported to be due to *P. vivax*, 25 to 30 per cent due to *P. falciparum*, of these 4 to 8 per cent are mixed infections with both. *P. malariae* has a restricted distribution and is said to be responsible for less than 1 per cent of the infections in India. *P. ovale* is a rare parasite of man.

Life Cycle of Malaria Parasite

The four species of malaria parasite in man differ from one another in structure but the general course of their life history is more or less similar. The malaria parasite undergoes two cycles of development: (1) the human cycle and (2) the mosquito cycle.

2

The Malaria Parasite

Only a female anopheles mosquito which has earlier bitten a malaria patient is in time, in a position to pass on the disease to another human being whom it bites subsequently. In the blood of a malaria patient are present the parasites of malaria which are the real cause of the disease. These parasites in the scientific language called plasmodia grow inside the body of the mosquito. Only after they have grown and multiplied in the mosquito and changed into another stage of the plasmodium are they capable of causing the disease in man.

The mosquito thus performs a very important

function in the causation of malaria by (1) letting the malarial parasite grow in its body and (2) passing it on to another person. The real culprit is the malaria parasite.

Let us get familiar with the parasites of malaria so that by recognising them and their potentialities we can take suitable steps in either not getting the disease or having once got it take measures to get rid of them from the body.

The number of known species of malaria parasite in man and animals is around 120. Only four species occur in man. These are (1) *P. vivax*, (2) *P. falciparum*, (3) *P. malariae* and (4) *P. ovale*. Of these, *P. vivax* has the widest distribution.

In India, 65 to 69 per cent of malaria fevers are reported to be due to *P. vivax*, 25 to 30 per cent due to *P. falciparum*, of these 4 to 8 per cent are mixed infections with both. *P. malariae* has a restricted distribution and is said to be responsible for less than 1 per cent of the infections in India. *P. ovale* is a rare parasite of man.

Life Cycle of Malaria Parasite

The four species of malaria parasite in man differ from one another in structure but the general course of their life history is more or less similar. The malaria parasite undergoes two cycles of development: (1) the human cycle and (2) the mosquito cycle.

Cycle in Man

This cycle begins when an infected mosquito bites a person and through its proboscis injects the malaria parasites in its developmental stage called sporozoites. The sporozoites are slender fusiform bodies. The number of sporozoites present in a single mosquito varies from perhaps a few hundred to several thousand. When a mosquito feeds the sporozoites which are mainly in the salivary glands are introduced into the body with the salivary secretion. Since the mosquito usually probes about with its proboscis until it strikes a small capillary the sporozoites are likely to be introduced directly into the blood stream and thus widely and promptly dispersed.



Sporozoites

The first phase in their development in human beings is in the liver cells. Here they reach from the

blood stream within half an hour of the bite of an infected mosquito and thereafter are no longer to be found in the peripheral blood. They develop, divide and mature in the liver cells for about 8 days in the case of *P. vivax* and 6 days in the case of *P. falciparum*. At the end of this development, these liver cells burst and out come the parasites which are now called *cryptozoites*. The stage when for the first time development of parasites occurs in the liver cells is called *primary exoerythrocytic stage*. The *cryptozoites* in all the species of malaria parasite except *P. falciparum* reinvade the other liver cells. This stage is called *secondary exoerythrocytic stage*. The two stages together being called the *tissue stages*. It may be noted that the *secondary exoerythrocytic stage* does not occur in *P. falciparum*. Further development of the parasites now occurs inside the red blood cells (*erythrocytes*).

The third phase begins when the *cryptozoites* attack and enter the red cells in the blood. They initially appear in these cells as minute blobs which soon takes the shape of a ring. The young trophozoite grows from the ring stage and in the case of *P. vivax* especially shows a good deal of mobility inside the red cells. Eventually it tends to round up and becomes less active. This rounded form is called *schizont*. Stained preparation of the blood at this time shows that nuclear substance, the chromatin of the parasite and the cytoplasm begin to divide, and

separate masses form which on maturity are termed as merozoites. Thus again for the second time—first time in the liver—the malaria parasite has divided and increased in number.

Now the infected red blood cell bursts and out come the merozoites in the blood. They pick up the nearest red blood cell and enter it and restart the cycle of division and increase in number—schizont formation—which again in time burst and more numbers of merozoites attack fresh red blood cells. This process may go on for days and months until the patient is treated or the immune response terminates further growth of the parasite. This stage of development is called the erythrocytic stage as it occurs within the red blood cells.

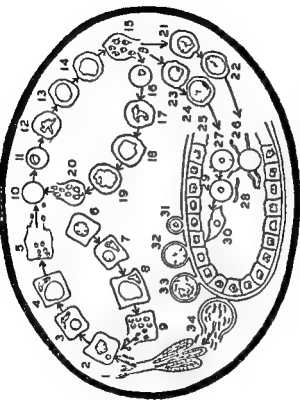
Some of the merozoites upon entering the red blood cells do not proceed through the cycle of schizont formation but proceed towards forming what are called the gametocytes, the sexual forms of the parasite. The trophozoites and schizonts are the asexual forms. Male gametocytes are smaller and are thus called microgametocytes and female are slightly larger and called macrogametocytes. More and more gametocytes are formed in the later course of the disease in man. Female gametocytes in the blood are much more in number than the male ones.

In *P. vivax* infection gametocytes appear in the blood 4 to 5 days after the appearance of the asexual zotes. In *P. falciparum* infections they take 10 to 12

days more. The gametocytes are incapable of developing further in the human. They can only develop now in the mosquito.

Mosquito Cycle

When a female anopheles mosquito bites a man who contains in his blood besides the asexual stages the gametocytes also, further development of the gametocytes begins. The asexual stages disintegrate in the stomach of the mosquito. Within ten or fifteen minutes the male gametocytes throw out 4 to 8 thread like filaments called microgamete, the process being called exflagellation. These remain attached to the parent cell for a few minutes, whipping about actively until they are liberated and swim away seeking the female gamete. The whole process can also be observed in blood on a glass slide under a cover slip. When a male gamete comes in contact with a female gamete, it enters into the latter, thus fertilising it. The resulting product called zygote becomes elongated and is called travelling vermicle or ookinate. It is mobile. It penetrates the inner stomach wall of the mosquito and develops into an oocyst on the outer surface of the stomach. Maturation of the oocyst takes a variable amount of time depending on the temperature, species and perhaps on the individual mosquito. A minimum of ten days time is required.



Life Cycle of Malaria Parasite

Life Cycle of Malaria Parasite

- 1 Sporozoites from salivary glands of mosquito entering liver cells
- 2 Liver cell containing early stages of primary exoerythrocytic parasite
- 3 & 4 Stages in development of the primary exoerythrocytic schizont in liver cells
- 5 Fully developed primary exoerythrocytic schizont rupturing and releasing cryptozoites
- 6 Liver cell containing cryptozoites of secondary exoerythrocytic cycle of the parasite
- 7 9 Stages in development of the secondary exoerythrocytic schizont in liver cell
- 10 Red blood cell
- 11 14 Stages in erythrocytic development [of the parasite]
- 15 Fully developed erythrocytic schizont rupturing and releasing merozoites and gametocytes
- 16 20 Repetition of erythrocytic schizont stage
- 21 & 22 Development of male gametocyte or microgametocyte
- 23 & 24 Development of female gametocyte or macrogametocyte
- 25 Stomach wall of the mosquito
- 26 Exflagellating microgametocyte producing microgametes
- 27 Macrogamete
- 28 Free microgamete
- 29 Zygote formed by fertilization of macrogamete by a single microgamete
- 30 Ookinete
- 31 Oocyst
- 32 & 33 Stages in the development of oocyst
- 34 Rupture of mature oocyst with release of sporozoites
- 35 Salivary glands of mosquito containing sporozoites

Symptoms of Malaria

Between the bite of an infected mosquito and the appearance of symptoms of malaria in the bitten person there is a time period during which the parasite is in the body. This is called the incubation period. For *P. vivax* it is 10 to 14 days, for *P. falciparum* 10 to 40 days, and for *P. malariae* 18 to 40 days. The incubation period is the time from the bite of the mosquito to the appearance of the first symptoms.

cells containing the mature schizonts of the malaria parasite rupture liberating into the blood the merozoites the malarial pigments and other material contained in the schizont. It is the appearance of them in the blood that causes a paroxysm of fever.

Classical Malaria Attack

The classical malaria attack has a sudden onset followed by four well marked stages (1) Cold (2) Hot (3) Sweating and (4) Apyrexial Interval when there is no fever.

Cold Stage

The patient first experiences a chill or rigor during which he feels very cold although his temperature is rapidly rising. Shivering may be so marked as to rattle the bed. Teeth chatter the skin is dry features pinched the extremities bluish tinged. The patient curls up in bed covering himself with all available blankets and still feels cold. The pulse is rapid but diminished in volume. There may be headache nausea and vomiting. This stage lasts from half an hour to about two hours.

Hot Stage

As shivering ceases the patient begins to feel hot.

3

Symptoms of Malaria

Between the bite of an infected mosquito and the appearance of symptoms of malaria in the bitten person there is a time period during which the parasite grows in the body. This interval is called the incubation period. For *P. vivax* infection it is 10 to 15 days, for *P. falciparum* 8 to 12 days, for *P. malariae* it is 30 to 40 days. The difference in the incubation period of the different species of the malaria parasite depends on the inherent difference in the human cycle of these parasites and the dose of infection of sporozoites.

An attack of malaria fever occurs when red blood

cells containing the mature schizonts of the malaria parasite rupture, liberating into the blood the merozoites the malarial pigments and other material contained in the schizont. It is the appearance of them in the blood that causes a paroxysm of fever.

Classical Malaria Attack

The classical malaria attack has a sudden onset followed by four well marked stages (1) Cold (2) Hot (3) Sweating and (4) Apyrexial Interval when there is no fever.

Cold Stage

The patient first experiences a chill or rigor during which he feels very cold although his temperature is rapidly rising. Shivering may be so marked as to rattle the bed. Teeth chatter, the skin is dry, features pinched, the extremities bluish tinged. The patient curls up in bed, covering himself with all available blankets and still feels cold. The pulse is rapid but diminished in volume. There may be headache, nausea and vomiting. This stage lasts from half an hour to about two hours.

Hot Stage

As shivering ceases, the patient begins to feel hot.

He discards the covers His face is now flushed eyes are suffused skin remains dry but hot and instead of appearing blue it may have a slightly pale tinge The pulse is full and bounding respiration rapid He suffers from increased headache rapid respiration parched throat coated tongue great thirst nausea and sometimes vomiting Slight delirium or euphoria may be noted Temperature may rise to 40 C or even higher during this stage This may last from 1 to 6 hours unless cut short by drugs

Sweating Stage

Rather suddenly the patient begins to perspire profusely first on face and hands then from every pore drenching garments and sheets He feels a great sense of relief his headache and vomiting cease his pulse becomes more normal he feels tired and drowsy and usually falls asleep with temperature normal or perhaps a little subnormal The sweating stage lasts 1 to 2 hours

The Aryrexial Interval

Following the sweating stage there is an interval of normal or slightly subnormal temperature when the patient may want to get up and carry on his usual activities although he is frequently somewhat pale weak and irritable with a poor appetite

After this apyrexial interval will come another cycle of chill fever and sweating unless the patient is treated in the meanwhile. Treatment may limit an attack to one or two cycles. Untreated patients may continue to have rigors for 10 days or longer before the infection lies low.

The periodicity of fever is dependent on the plasmodial cycle since rigors coincide with the bursting of schizonts present in the red blood cells.

Each of four causative species of malarial parasite presents its own characteristic features which are as follows.

Vivax Malaria (Benign Tertian)

While first attacks may be classical from the onset, it is more common in a primary episode to see a daily rise in temperature in *P. vivax* infection before the 48 hour periodicity becomes established. Such daily rise of fever may be due to two broods of parasites coming out of the liver cycle. The fever may rise upto 39°C and above. Cerebral symptoms are not common in *P. vivax* malaria but one sometimes encounters dizziness, drowsiness, transitory disorientation or syncope. Intestinal symptoms are also likewise not the rule, aside from some abdominal discomfort and occasional diarrhoea.

Spontaneous relapse is usual in vivax malaria, frequently within one month but sometimes consider-

ably delayed There is much greater tendency for vivax malaria to relapse than in the case of falciparum infections But vivax malaria is seldom fatal, even when untreated

In children vivax malaria often does not show typical periodicity The fever may be slight and irregularly discontinuous Convulsions are more common than in adults Progressive anaemia and marked enlargement of the spleen are usual in untreated cases

Blood smears are generally positive throughout the apyrexial period in untreated cases

Malariae Malaria (Quartan)

The paroxysm occurs usually after 72 hours The paroxysm is generally no more severe than in vivax infection although the rigors may be more exhausting The paroxysms are generally more regularly spaced

This has marked tendency to relapse and this may lead to clinical episodes three or four or even more years after the infection was contracted Kidney involvement (nephritis) is reported to occur more commonly with this than with *P. vivax* or *P. falciparum* infection

Ovale Malaria (Tertian)

It resembles vivax infection but is milder with a

tendency to early latency and much less liability to relapse

Falciparum Malaria (Sub-Tertian or Malignant Tertian)

A frank chill may not occur in falciparum infections but only slight chilliness followed by a prolonged hot stage and much less sweating. The paroxysm is likely to be more exhausting than that of either vivax or malariae. Irregularity in the course of the paroxysm, which may last from 30 to 36 hours is typical of falciparum infections. There is more prostration, headache is more severe, vomiting more frequent, mental confusion and stupor more common.

There may not be a well marked apyrexial period. Temperature may rise and fall gradually rather than suddenly. A temperature of 39°C or more should be considered as a serious sign in falciparum malaria.

Blood in falciparum infections may not show the parasites. This is because the parasite infected red blood cells are held back in the capillaries of the spleen or other organs soon after young ring forms begin to broaden.

Fulminant or Severe Malaria Attack

Fulminant attacks of malaria as a rule occur

only in recently infected individuals or those experiencing early relapses, because such patients have not developed immunity to the parasite. This occurs nearly always due to *P falciparum* as this species surpasses others in its ability to multiply and cause subsequent changes in the body.

Under epidemic conditions fulminant attacks may occur both with *P falciparum* or *P vivax*.

In fulminant infections the clinical picture may be grouped under three headings depending upon the predominant localization of symptoms and signs. These are (1) the Nervous System (2) the Gastro-Intestinal System and (3) elsewhere.

Cerebral Malaria

The onset of cerebral malaria varies greatly and may be gradual or sudden. For instance a man may be seen in the out patient clinic in the morning without fever and complaining only of headache but he may be brought in coma with fever in the afternoon. Patients may be found in malaria coma an hour or two after the ward rounds when they had seemed normally responsive. Fever, headache, vomiting, sighing respiration, full rapid pulse, stiff neck may be noted. Other indications of cerebral malaria are excitement, disorientation, somnolence and coma. The patient may be stimulated to answer

a question but then sinks back into deep stupor. High fever and shock may develop.

Gastro-Intestinal Malaria

Intestinal localization of symptoms may lead to so-called algid or cold malaria with sudden collapse some times without other symptoms but more often associated with bloody vomitus, muscular cramps, suppression of urine and blood and mucus in stool. Cholera like symptoms may develop without a typical rigor or any of the familiar symptoms and signs of malaria.

Malaria in Children

Malaria is rare in the first few months of life. An acute attack of malaria in children does not resemble the disease in adults. Fulminant forms are more often seen. Besides *P. falciparum* even *P. vivax* is known to cause them. The onset is often gradual, the child becomes dull, restless, resenting feeding and often vomiting, sometimes the vomitus being blood stained. Abdominal pain, flatulence and diarrhoea are common. Temperature ranges between 38 to 40 C and the fever may be continuous or coming on at intervals. Rigors are not common but there may be stiff neck and convulsions when the fever is high. Anaemia develops more rapidly. Death due to

fulminant malaria is more common in children than in adults

Malaria in Pregnancy

Malaria can prove serious in pregnancy. It may cause miscarriage or abortion. It may be an important predisposing factor of complications of pregnancy such as eclampsia. Special care should be taken to protect pregnant women from malaria and to detect malaria in them and to treat it promptly.

Although a majority of patients suffering from malaria present a characteristic triad of intermittent fever, anaemia and splenic enlargement, yet few diseases have as wide a range of clinical syndromes as malaria. Factors such as epidemic conditions, acquired immunity, mixed infections with more than one species of malaria parasite, previous clinical and suppressive treatment, all modify individual response, the clinical picture and the course of the disease.

Malarial Emaciation

The most serious result of repeated attacks of malaria is malarial emaciation, which is characterized by severe anaemia, emaciation and great physical weakness, a condition which is not chiefly as a result of poor memory, spleen in

enlarged, sometimes extending into the pelvis. The liver too is often enlarged. The spleen is susceptible to rupture or to twisting. Loss of appetite and mild diarrhoea are common. Anaemia may lead to shortness of breath and palpitation. Amenorrhoea is not uncommon in women. Abortion frequently occurs in the presence of malarial emaciation.

Blackwater Fever

This is one of the manifestations of malaria occurring more often in previously unexposed people coming to reside in a malarial epidemic area. There is fever for which the patient may have taken quinine. A short while later the patient passes dark red or black urine. He has vomiting and pain in the loins. Within a few hours more than half the number of red blood cells may get destroyed (haemolysed). Mild cases may recover but those who pass into the stage of cessation of urine formation and shock may not recover.

fulminant malaria is more common in children than in adults

Malaria in Pregnancy

Malaria can prove serious in pregnancy. It may cause miscarriage or abortion. It may be an important predisposing factor of complications of pregnancy such as eclampsia. Special care should be taken to protect pregnant women from malaria and to detect malaria in them and to treat it promptly.

Although a majority of patients suffering from malaria present a characteristic triad of intermittent fever, anaemia and splenic enlargement, yet few diseases have as wide a range of clinical syndromes as malaria. Factors such as epidemic conditions, acquired immunity, mixed infections with more than one species of malaria parasite, previous clinical and suppressive treatment, all modify individual response, the clinical picture and the course of the disease.

Malarial Emaciation

The most serious result of repeated attacks of malaria is malarial emaciation, which is characterized by severe anaemia, emaciation and great physical weakness, a mental disturbance which is manifested chiefly as inability to concentrate, poor memory and a tendency to be depressed. The spleen is usually

enlarged, sometimes extending into the pelvis. The liver, too, is often enlarged. The spleen is susceptible to rupture or to a twisting. Loss of appetite and mild diarrhoea are common. Anaemia may lead to shortness of breath and palpitation. Amenorrhoea is not uncommon in women. Abortion frequently occurs in the presence of malarial emaciation.

Blackwater Fever

This is one of the manifestations of malaria occurring more often in previously unexposed people coming to reside in a malarial epidemic area. There is fever for which the patient may have taken quinine. A short while later the patient passes dark red or black urine. He has vomiting and pain in the loins. Within a few hours more than half the number of red blood cells may get destroyed (haemolysed). Mild cases may recover, but those who pass into the stage of cessation of urine formation and shock may not recover.

Pathological Changes in the Body

Changes in the body are initiated when the parasites invade the body and proceed to multiply within red blood cells. Because of their localisation in the blood vessels of the internal organs *P. falciparum* infections bring about marked pathological changes. The changes produced may be described as follows:

Blood

A constant feature of malaria is destruction of red blood cells. This occurs when infected red blood

cells rupture after proliferation of the parasites in them. It also occurs through engulfing (phagocytosis) of infected as well as normal red blood cells in the spleen and liver. Red blood cell debris stimulates production of toxins which destroy further the red blood cells.

In an acute malaria attack, the haemoglobin is generally reduced in amount in direct proportion to the loss of red blood cells. Chronic malaria is more likely to be characterized by markedly reduced haemoglobin with a moderately reduced red cell count.

Though changes occur in the white cells also except for the presence of malaria pigment in them these are not characteristic of the disease.

In the plasma albumin is reduced and globulin increased. The peculiar globulin increase sometimes causes the serological tests for syphilis to be positive. This may remain so far as long as four weeks. This phenomenon has to be properly understood otherwise it may lead to false diagnosis of syphilis.

Spleen

One of the functions of the spleen is to recognize, filter out and phagocytose old or abnormal red blood cells. In cases of malaria, the spleen filters the parasitized red blood cells and the debris of the dead cells. As the spleen has a lot of phagocytosing

work at hand in cases of malaria the cells which perform this function increase in number

During each paroxysm of malarial fever the spleen becomes swollen and tender. Almost invariably in untreated cases it becomes palpable three or four days after the beginning of an acute attack. It subsides rapidly during treatment and is thus not so frequently palpable in those who have had adequate treatment.

Repeated infected infections result in a greater degree of spleen enlargement than that following a single infection even though attack periods are of equal duration. After long continued malaria especially in *P. vivax* infections the spleen may weigh as much as 5000 gms or more. The average normal weight of spleen is around 200 gms. The covering and the inside of the spleen shows characteristic microscopic changes in cases of malaria.

Liver

Enlargement, tenderness and impairment of liver functions occur in cases of malaria. It changes in colour, turning slaty blackish in appearance and firm even hard. Microscopically liver structure shows characteristic changes in malaria.

Capillary Occlusion

In case of falciparum malaria, there is an enormous proliferation of the parasites inside the red blood cells. The masses of agglutinated parasitized red blood cells cause capillary blockage in many organs of the body. These and other changes occur in the brain, spleen, liver and other organs as well.

Brain

In fulminant infections with *P. falciparum*, cerebral malaria, the capillaries are full of masses of parasitized red cells, malarial pigment, phagocytic cells and occasionally free parasites, sometimes giving the appearance of thrombi or clumps. Other changes in the brain consist of small haemorrhages and small degenerative foci.

Characteristic malarial changes also occur in the gastro-intestinal tract, pancreas and the kidneys.

Skin

Skin becomes pale, sallow, showing small patches of pigmentation. Some patients with acute malaria have severe herpes labialis and others with chronic malaria may have a considerable degree of urticaria. Petechial haemorrhages and sometimes purpuric spots are occasionally reported in malaria.

5

Diagnosis of Malaria

The only certain diagnosis of malaria is made by demonstrating the malaria parasite. This is done by making a thick and thin film of the patient's blood and after staining the blood film and examining of the same under the microscope.

Blood Smear Examination

Living in a malarious area it becomes the duty of all responsible citizens to know how to make a blood slide. A doctor may not be available when needed and a blood smear made at the time of

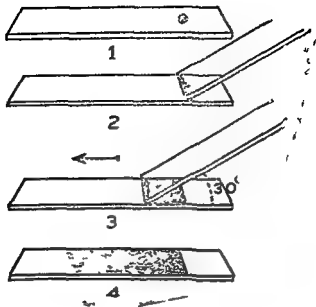
rigor or at any stage of the fever before treatment is given is necessary. All it needs is keeping a few glass slides in the home and learning the simple technique.

For making blood smears the material required is two clean glass slides, a needle, a cotton swab and methylated spirit.

Clean the tip of the middle finger (or big toe in case of infants) with cotton swab soaked in methylated spirit and then let the spirit dry. With a sterile needle or one which has been passed through flame and cleaned with spirit, a sharp prick is given. The finger tip is squeezed gently and if the prick given has been adequately deep, out flows a thick drop of blood.

For making of the blood film, the glass slide should be meticulously clean, free of dust, grease and scratches. A large free flowing drop of blood is allowed to touch on the outer third of the slide and is rapidly spread with the pricker to form a round or square thick smear about 1 cm in diameter. This thick film should dry by itself without exposure to any undue heat and must be protected from dust, flies, ants and cockroaches.

If possible, a thin film should also be prepared on the clean part of the slide. A small drop of blood is placed near the centre of the slide and the slide is laid on the table. The blood is touched with



Making of a blood film

the narrow edge of another clean slide held at an angle of 30° . As soon as the blood spreads along the edge this slide is pushed along the surface of the first slide to form a thin and even film.

It is desirable to have the thick and thin film on the same slide as it allows for a better identification of some species of malaria parasites and mini

mizes various technical errors

Blood films should be made even if they cannot be examined immediately

The malaria parasites are the greatest in number in blood a few hours after the rigor With *P vivax* infection blood smear is usually positive for the parasite but in *P falciparum* infections this may not be so Hence in a case of continuing fever which clinically is suspected to be that of malaria it is necessary that blood smears be examined repeatedly Reliance on negative results may lead *P falciparum* infections to the stage of coma

Since examination of blood smears takes time, considerable experience and devotion to work it is necessary that the technicians employed for the job be such that the reliability of their report can be depended upon

From the examination of blood smears in a malaria patient it is possible to establish the species of the infecting malaria parasite

Suggestive Clinical Findings

Clinical findings most constantly associated with malaria with or without a positive smear are

- 1 Fever especially when it comes up and goes down (intermittent) with rigor and sweating
- 2 Anaemia
- 3 Enlargement and tenderness of spleen The spleen may become palpable a few days after

onset of symptoms Sometimes there is tender-
ness of the spleen before the organ is palpable

4 History of potential exposure to infection or of
previous malaria

The diagnosis of malaria cannot be ignored be-
cause of a typical symptoms Double or multiple
infections with the same species of malaria parasite
and mixed infections especially a combination of
P vivax and *P falciparum* are common in times of
epidemics These complex infections lead to a typical
clinical picture

Irregular suppressive treatment also may greatly
modify clinical picture The only symptoms may be
persistent headache backache or eye disturbances with
pain If all specific antimalarial treatment is with-
held blood smears may become positive after 3 to
6 weeks at which time a typical attack of malaria
may be witnessed

Differential Diagnosis

The diseases which may be kept in view in a
case of fever and which should be excluded before
a diagnosis of malaria is established are influenza
dengue typhoid infectious hepatitis amoebiasis
with liver abscess filariasis kala azar septic infec-
tions

Diagnosis of influenza is made upon the clinical
symptoms and from the fact that an epidemic of it

is around Before making this diagnosis, it is essential that the blood be examined for malarial parasite if the patient is living in a malarious area Laboratory confirmation of the diagnosis of influenza takes much time

In dengue one frequently notes severe generalized muscle pain saddle-back seven-day fever curve, slow pulse lymph gland enlargement rash, marked fall in white blood cell count None of these occur in malaria As in a case of influenza diagnosis of dengue should be made only after exclusion of malaria

In typhoid fever one depends on early stool culture and later on Widal tests for definitive diagnosis Negative blood smears and lack of response to malaria therapy also help

Differentiation between malaria and the pre jaundice stage of infectious hepatitis may be difficult Tenderness of the liver is more pronounced in infectious hepatitis

Amoebic abscess of the liver must be differentiated from malaria Enlargement of the liver without splenic enlargement rigidity of the right rectus abdominal muscle fever increase of white blood cells with 70 to 80% polymorphs all suggest the possibility of liver abscess Clinical response to specific treatment with emetine is another diagnostic point Confirmation of diagnosis by X rays or by an exploratory puncture may be possible

or marks of insulin injections on the patient's body

In alcoholic coma the patient smells of liquor
In opium coma there is no fever

6

Anti Malarial Drugs

There would hardly be any substance or procedure that has not been used through the ages against malarial fevers ' From wearing a spider hung around one's neck in a nutshell or placing the fourth book of the *Iliad* under a patient's bed to taking snuff of a tallow candle on sugar bread and butter or seven sages leaves on seven mornings fasting and down the years through massive calomel purges to colloidal gold no suggestion has been too bizarre for written testimonial '

Malaria has invited this flow of therapeutic suggestions by reason of its great prevalence throughout the

world and because it is a disease that tends to be self limited. The patient may recover from acute episodes without treatment or following the administration of almost any medication.

Yet the list of truly useful antimalarial drugs is a short one. This includes quinine, mepacrine, chloroquine and amodiaquine, primaquine and proguanil and pyrimethamine. The following description indicates for which stage/stages each of these drugs is effective. The dosages, toxicity and other relevant particulars are also given.

Quinine

Quinine, an alkaloid derived from cinchona bark, interrupts the development of malarial parasites of all species and at all stages in the red blood cells, except those of gametocytes of *P. falciparum*. It has no effect on exoerythrocytic stages of the development of the malaria parasites. Now a-days it is chiefly used as the drug of choice in chloroquine resistant strains of *P. falciparum* infections.

Quinine is given orally as its sulphate at intervals of 6 to 8 hours as it is not stored in the body. It is rapidly and completely absorbed from the gastrointestinal tract. Injected intramuscularly it is not more quickly absorbed than given orally, but former is the route resorted to in cerebral malaria cases which are comatose. Intramuscular injection can

produce extensive tissue damage unless due care is taken. Intravenous injection needs to be given very slowly. It is likely to cause convulsions sometimes.

The toxic symptoms produced as a result of giving quinine include one or more of the following: tinnitus, deafness, dizziness, changes in vision, nausea, vomiting, diarrhoea, urticarial rash. These symptoms are usually mild and disappear after treatment is stopped. But in case the drug is given in overdosage or continued too long, permanent damage may occur to the ears and the eyes.

Mepacrine

Synthesized in Germany in 1930, it gained world wide popularity. Its action is like that of quinine. It destroys all malaria parasites of all species developing inside the red blood cells except the gametocytes of *P. falciparum*. Gametocytes of *P. vivax* disappear more rapidly from the blood after its administration as compared with quinine. Because of its rapid destructive action on schizonts, it tends to eliminate *falciparum* gametocytes by bringing an end to schizogony.

Mepacrine given orally is rapidly absorbed in the blood. It takes longer to attain optimal blood level as it has a tendency to localize in various tissues of the body.

Mepacrine is relatively non-toxic. Some patients

may complain of anorexia salivation nausea vomiting diarrhoea headache and restlessness Prolonged administration gives a yellowish tinge to the skin

Because it causes yellowish tinging of the skin ■ longer time to reach optimum effective level in the blood its use has now a days been superseded by new more effective and less toxic drugs

Chloroquine and Camaquine

Chloroquine was first synthesized in Germany in 1934 and was named Resochin Both chloroquine (4-aminoquinoline) and camaquine (amodiaquine) like quinine and mepacrine are active against all species of malaria parasites in red blood cells except the gametocytes of *P falciparum*

They are not active against exoerythrocytic forms of the parasite In an acute attack they rapidly destroy parasites in the blood and abate the clinical symptoms in most patients temperature touches normal within 24 to 48 hours and blood smears become negative in 48 to 72 hours

Chloroquine and camaquine are rapidly and almost completely absorbed from the alimentary tract and are localized in various tissues from which they are slowly metabolized and excreted Given intramuscularly chloroquine becomes concentrated in the plasma in therapeutic amounts within 15 minutes

Chloroquine and camaquine have largely replaced

quinine and mepacrine in malaria treatment because (1) they act more promptly on the erythrocytic forms and thus bring down fever more quickly (2) they lengthen the period when the patient may not get a subsequent attack, (3) they do not tint the skin and (4) they have low toxicity

Primaquine and Pamaquine

Pamaquine (8 aminoquinoline) was synthesized after the First World War. It is more toxic than primaquine though both have similar action on different stages of development of the malarial parasites.

The speciality of primaquine is that it is active against secondary exoerythrocytic forms of *P. vivax*. Because of that it is the most important drug available for radical cure of vivax malaria after the fever has been halted. Radical cure implies clinical cure plus elimination of malaria parasites from the liver so that relapses do not occur.

Primaquine is rapidly absorbed orally and rapidly eliminated.

Unfortunately primaquine is a fairly toxic drug. Symptoms of primaquine toxicity include abdominal pain, nausea, vomiting, headache, dizziness and drowsiness. Less common but more significant toxic effects are destruction of red blood cells (haemolysis) and passing of dark coloured urine as a result of that. The tendency for haemolytic reaction following

7

Treatment of a Malaria Attack

In an area where malaria is known to occur commonly all cases of fever—after the blood smear has been made—are recommended by some doctors to be treated as malaria. In the majority of the cases of malaria the fever thus comes down within twelve to twenty four hours. It is only after the fever does not come down in this duration that the patient is investigated further. In the meanwhile the result of the blood smear of the patient also becomes available so that if malaria is confirmed and the species of malaria causing the disease known a further course of action can be adopted if necessary.

The initial treatment of a malaria patient is the same irrespective of the species of malaria parasite that is causing the disease. Additional follow up treatment is necessary in the type of malaria where relapses are known to occur as in cases of *P. vivax* and *P. malariae* infections.

For an attack of malaria either chloroquine (Nivaquine) or camaquine are the drugs of choice. The National Malaria Eradication Programme (NMEP) recommends an adult's dose of only four tablets of chloroquine or camaquine to be given at a time. Fever comes down in twelve to twenty four hours in an acute attack of malaria.

In case the patient is suffering from *P. falciparum* malaria this is all that is required to be done. In case it is found that the infection was due to any of the other three species particularly the *P. vivax*—which is the most common infection in most parts of the country—then a further course of another drug namely primaquine in an adult dose of 15 mg a day for 5 days is recommended to be given after the fever has come down.

The advantage of taking radical treatment with primaquine is that the patient suffering from these types of malaria ensures that he will have no relapses which weaken the patient very much and make him susceptible to other diseases.

Primaquine in the doses prescribed rarely causes

severe toxic symptoms of red blood cells destruction. Recognition of the defect in the metabolism of the enzyme glucose 6 phosphate dehydrogenase ■ an added precaution before this drug is given.

If primaquine is given under strict medical care and the patient is cautioned to stop the drug and report at once to the doctor if nausea, vomiting and dark coloured urine is passed, the dangers of primaquine administration can be minimised.

Quinine is not used now a days in the treatment of an attack of malaria unless the species of malaria infecting a patient is non responsive to chloroquine and has become resistant to it.

Drug resistance is suspected when cases of malaria usually *P. falciparum* infection do not fully and rapidly respond to standard treatment with chloroquine or when recrudescence of symptoms occur and parasites are seen in the blood soon after their temporary disappearance or coming to low level subsequent to therapy.

The above mentioned drugs are bitter and should be given along with a drink of milk, fruit juice, other flavoured fluid or a glass of water after food and not on empty stomach. Care must be taken to make certain that the patient swallows the tablets and they are not vomited out.

As regards the general treatment of the patient during acute attacks of malaria, the patient should remain in bed. If body temperature rises above 39°C

ice cap or sponging is necessary Nausea may be alleviated by sucking ice Muscular pains are relieved by taking acetylsalicylic acid or paracetamol Fluid intake should be maintained at three or four litres daily and salt loss made up

Since the diagnosis of the disease can be made only by an experienced doctor his advice in the matter is essential Self medication is likely to lead to inadequate or incorrect treatment in a case of malaria in case it is not malaria it will lead to delay in correct diagnosis and complicate the case

If the advice of a doctor is not immediately available a person living in malarious area getting fever with symptoms akin to malaria may take 4 tablets of chloroquine as the fever comes up It is advisable that he makes a smear of his blood on a clean glass slide to be examined later on

8

Treatment of Cerebral Malaria

Irrespective of the species of malaria parasites causing the disease any severe malarial infection with cerebral symptoms vomiting pronounced nausea or defective absorption from gastro-intestinal tract requires parenteral administration of a rapidly acting anti malarial drug In *P falciparum* infection even though clinical symptoms may not be very alarming the patient should be treated as a medical emergency Preferably the patient should be transferred to the hospital for dealing with any complication that may develop with dramatic suddenness

Chloroquine and quinine are the best drugs for parenteral administration. Intravenous injection acts somewhat more rapidly than intramuscular injection but presents a relatively greater risk in some patients. Quinine is given if resistance of the parasite to chloroquine is suspected.

For an intravenous injection 200 mg base of chloroquine diphosphate in 20 ml of normal saline or distilled water is injected very slowly and the injection completed in not less than 15 minutes. If the patient is in a state of shock 200 mg of chloroquine diphosphate should be given by intravenous drip in half a litre of 5 per cent glucose saline. If there is no appreciable improvement in 8 hours the second dose can be given.

Unless there are good clinical indications for intravenous administration of chloroquine intramuscular route can be employed. Chloroquine diphosphate 200 mg of the base should be made in 9 ml of sterile normal saline or distilled water and injected into gluteal muscle. Readymade chloroquine (Resochin) ampoules are also available. It can be repeated at 8 hourly intervals in first 24 hours.

Intravenous quinine must be given in high dilution. Quinine dihydrochloride solution is given in the adult dose of 8 to 10 mg of body weight (500 mg) diluted in 20 ml of glucose saline. It should be injected very slowly in at least ten minutes. If the

patient is in shock it should preferably be given as an intravenous drip in 0.5 litre of glucose saline. This may be repeated if necessary after six to eight hours. The total dose in 24 hours should not exceed 2000 mg.

For intramuscular injection quinine hydrochloride 500 mg made in 9 ml of normal saline or distilled water is injected into gluteal muscle.

As with many other drugs faulty technique of intravenous injection of quinine or chloroquine solution may produce local necrosis of surrounding tissues; this risk is greater with quinine than with chloroquine.

The proper technique of intramuscular injection, especially that of quinine, must be strictly observed. After a thorough cleaning of the skin the drug should be given in the classic site of the upper external quadrant of the buttock deep into the gluteal tissue. Sterile precautions must be strictly observed to avoid accidental contamination. Quinine injections may produce local transient reactions which occasionally leave long lasting fibrotic indurations. This is exceptional with chloroquine.

Intravenous injections of any anti-malarial drugs in children below seven years of age may be dangerous and should be avoided if possible. Intramuscular injections should be given only when really necessary in severe infections requiring rapid treatment and the dosage of the drug must be based on

the weight of the child. It is safer to give the drug in two halves separated by an interval of one to two hours. Oral treatment of all cases of malaria should be preferred and used wherever possible.

Shock, coma or convulsions are promptly treated by standard procedures.

In cerebral malaria the patient develops very high fever. He should be wrapped in a wet sheet, immersed in cold water and placed under a fan. If possible, he should be moved to an air conditioned room. Injection paracetamol 0.5 gm intramuscularly is given, which can be repeated after 8 hours. Temperature is recorded rectally.

Drug Prophylaxis or Suppression of Malaria Attack

Drug prophylaxis or suppression implies prevention of clinical symptoms of malaria even though the person has been infected by malaria parasites. This is resorted to in certain circumstances.

A person bitten by an infected mosquito develops in his body exoerythrocytic stages of the malaria parasites in the liver and also erythrocytic forms inside the red blood cells. If he is not to get an attack of malaria the malaria parasite should be killed before the red blood cells containing merozoites burst forth.

The drug commonly used for the prophylaxis of malaria is chloroquine which kills parasites in erythrocytic stages of all the species of malaria. Chloroquine is toxic after prolonged use and not suitable drug but this needs to be taken once a week. Since repeated infections are liable to occur in malarial areas the drugs need to be taken repeatedly.

The drugs used for prophylactic purposes and their dosage schedule are as follows in adults and proportionately less in children.

Chloroquine—300 mg (2 tablets) once a week

Proguanil (Paludrine)—300 mg tablet weekly

Pyrimethamine (Daraprim)—25 mg twice a week

The dose of chloroquine compared to the adult dose for children and infants is as follows: children between 11—16 years $\frac{3}{4}$ dose, 7 to 10 years $\frac{1}{2}$ dose, 4 to 6 years $\frac{1}{3}$ dose, 1 to 3 years $\frac{1}{4}$ dose and under 1 year $\frac{1}{8}$ dose.

A traveller passing through a malarious area should take prophylactic anti-malarial drugs preferably one week before arrival or take initial double dose in 2 divided doses 8 hours apart.

After leaving the malarious area it is very important to continue drug prophylaxis for at least 4 weeks and preferably 6 to 8 weeks.

Pregnancy is not a contraindication to the use of anti malarial drugs

At the appropriate dosage none of these drugs has any serious side effect

Drug prophylaxis is essential for more vulnerable groups such as children or pregnant women

Use of prophylactic antimalarials for each and every person living in a malarial area is not recommended. The symptoms and signs of malaria are fairly well recognized and an ordinary attack of malaria is not too serious a thing. Why not take just 4 tablets of chloroquine when the fever occurs rather than to go on taking 2 tablets of it every week?

Difference of opinion on recommendation of drug prophylaxis does occur. It seems that where and when malaria is less prevalent drug prophylaxis may be omitted if however the incidence of malaria is very high in a particular area and at a particular time so that the chances of frequent infections exist drug prophylaxis may be taken regularly.

Malaria Immunity and Vaccination

Immunity

Malaria whether treated or not tends to be self limited. The primary attack may be followed by complete recovery or by a series of latent periods alternating with relapses the former tending to be come progressively longer and the latter less and less severe until cure occurs. In vivax malaria, it has been observed that a clinical attack usually terminates in the presence of a considerably higher parasite counts in blood than that sufficient to initiate the attack. Most attacks occur with parasite

counts between 10 and 100 per c mm yet clinical activity usually terminates spontaneously at counts of from 1000 to 5000 parasites per c mm. Furthermore, the onset of relapses is generally marked by considerable higher parasite counts than seen in primary attack. This shows an acquired state of immunity against the malaria parasites.

The development of this immunity is most evident in highly endemic areas where people are completely unprotected against almost nightly infection. At a cost of high infant and child malaria death rates these people succeed in 10 to 15 years in developing a marked immunity to malaria. It is manifest by absence of severe clinical attacks among adults and prevalence of infected persons with no symptoms. This immunity is however not absolute in fact one can almost always find adult cases of clinical malaria in highly endemic areas.

This immunity results because of certain cells called macrophages as well as the production of special kind of proteins called immunoglobulins which are the antibodies. The cells are normally found in the spleen, liver and bone marrow etc. They are meant to engulf and digest foreign material from the blood stream. With repeated attacks of malaria these cells increase in number and their activity.

The exoerythrocytic stages of malarial infection do not seem to be accompanied by any recognizable

increase of immunity possibly because of the short life of injected sporozoites in the circulation and their subsequent relative isolation in the liver. In contrast erythrocytic infections are followed by increased immunoglobulin synthesis and the production of malaria antibodies which can be detected by a variety of immunological techniques. The antibodies increase until the crisis and then slowly decline. But they are still usually apparent many months after the infection and may reappear in greater density after relapses. Antibodies against *P. falciparum* may persist for 8 years and against *P. malaria* for up to 26 years but for only 3 years after *P. vivax*. A particular type of immunoglobulin called IgG seems to correlate well with malarial infection in man.

Vaccination

The concept of immunization against malarial infection is of great potential value in the eventual conquest of the disease just as it is in other communicable diseases. This is particularly so in view of the increasing spectrum of drug resistance of parasites to drugs and of mosquitoes to insecticides. Making of a vaccine against malaria however, presents technical problems in view of the different stages in the development of the parasite both in man and mosquito. Furthermore many species of

11

Prevention of Malaria

Malaria occurs when a female anopheles mosquito which has previously sucked the blood of a patient having malaria parasites subsequently bites another person. If either the biting mosquito or the malaria parasite be eliminated malaria would not occur.

In order to check the bite of a mosquito either the mosquito should be eliminated or the person protected against its bite.

The number of mosquitoes present in an area can be controlled by either preventing the mosquitoes from breeding or by killing the adult ones.

In actual practice all the three above mentioned

measures need to be taken so that human beings are protected from the mosquito bite. These are

- (1) Control of mosquito breeding
- (2) Control of adult mosquitoes and
- (3) Protection against mosquito bite

Let us see how these three measures can be implemented

(1) Control of Mosquito Breeding

The intention in preventing mosquito breeding is to limit the number of adult mosquitoes hatching out

The measures adopted for controlling breeding of mosquitoes can be categorised under the following heads

- A Elimination of breeding places
- B Oiling over the breeding places
- C Use of Paris Green
- D Use of synthetic insecticides
- E *Biological control of mosquito breeding*

We shall take up each of these measures individually

A Elimination of Breeding Places

The ancient Greeks and Romans drained marshes empirically in order to be rid of noxious vapours which seemed to cause chills and fevers. Drainage of

breeding places of mosquitoes is still the most important measure to check their breeding

A great part of *malaria* and particularly of the epidemic form has been due to the neglect or ignorance of man who has time and again created breeding places for mosquitoes. These places have been created through interference with drainage lines the creation of pools such as burrow pits often in great abundance the impounding of water in reservoirs, its wide distribution typically in irrigation projects, and the creation of *miscellaneous collections* such as seepages waste water collection and cart tracks in the villages

Perhaps the most important activity in this connection is modification of drainage lines in the construction of roads railways and canals. The embankments on which they stand restrict the flow of water. Its prevention lies in the provision of sufficient and adequate culverts set low enough below surrounding ground level to provide a run off for water. This type of construction is also usually accompanied by the construction of innumerable burrow pits separated from each other

Areas so low that they cannot be drained by simple run off ditches may require pumping. Small portable pumps are used for the purpose in and around the city. The water is pumped either into a ditch or out over a wide flat area where it will evaporate or be


absorbed before becoming a breeding place of mosquitoes. Such mosquito control is however only a temporary expedient. Filling of the depressions where water collects is a more permanent measure.

Some epidemics of malaria in Delhi have been reported among the inhabitants of the slums that formed where multi story construction was going on. Mosquito breeding has been known to occur in the water which is either intentionally collected or gets inadvertently collected in such places.

In and around the cities the largest number of places where the mosquitoes breed are the desert coolers in the houses which are left unused full of water when the rainy season starts. Thousands of breeding places for the mosquitoes are thus provided over which the health authorities have little control. This has to be individually looked into by each householder for the care of his or her own health as well as of the neighbours.

Breeding of mosquitoes can occur in innumerable small undisturbed places where water is left undrained e.g. in flower vases inside the house on the roof tops and in places around the house. It is the duty of all of us to see that this does not happen.

B. Oiling Over the Breeding Places

Oil is a rapid destroyer of mosquito larvae and pupae. When applied on water it spreads a  thin

spray and in the rural areas with synthetic insecticides like DDT, BHC dieldrin lindane and malathion. These insecticides are sprayed on walls and ceilings of human dwellings and cattle sheds where the mosquitoes are likely to rest.

Resistance to these compounds has become common among the mosquitoes.

Resistance of the mosquitoes to DDT has been reported and also it has been reported that its cumulative effect is toxic to human beings and other animal life. Yet in the absence of an ideal insecticide which is less expensive, adequately effective with long lasting action, DDT is the one which is still depended upon to do the job. An eminent malariologist has stated that DDT today is like a rather rich but erratic aunt. We know all about her deeds and misdeeds but we still prefer to have her because she has been so good to us in the past and still provides us an effective insurance against disaster in the immediate future. DDT in spite of all that is said against it in affluent countries continues to be the main reliable weapon against vector borne disease, like malaria, in developing countries.

Frequent spraying inside the houses with fit and allied preparations checks the number of mosquitoes inside the houses.

Pyrethrum sprays inside the houses are effective only for a short while. DDT and allied sprays are

effective for a much longer time because of their residual effect

In recent years genetic methods have shown promise for the control of mosquitoes in laboratory and field trials. The genetic method used is the sterile male technique. The male mosquitoes are sterilised in the pupal stage by exposure to gamma radiation or to chemicals. The sterilised males are released in large number exceeding the males in a natural population. They compete successfully for local females whose eggs fail to hatch resulting in the control or eradication of the species. This method has certain advantages over chemical methods being cheaper and potentially more efficient and above all not subject to vector resistance. But it is difficult or almost impossible in a huge country like India.

Lessening the number of mosquitoes in our surroundings is a sure method of lessening the incidence of malaria.

Protection Against Mosquito Bites

Different methods are recommended for the purpose.

A Wearing Protective Clothing Veiling the head as a measure of protection from mosquito bite has been helpful in some areas. *Sarongs* or pillow slips are effective temporary leg covers for thwarting mosquitoes. It is said that they were at one time regularly

Such specifications have not yet been met although many substances have been tested. The fact that so many chemicals have been tried suggests at once that none of them proved satisfactory.

Certain new products have been developed which are much more useful than any of the older materials. Diethyltoluamide has been found to be an outstanding one. Others are Indalone, dimethyl phthalate, dimethyl carbate, ethyl hexamediol, etc. They are fairly effective for up to a maximum of three to four hours.

The most commonly available material in India is dimethyl phthalate which is made up into cream.

Use of mosquito repellent cream is liable to give a false sense of protection. Applied at 9 or 10 p.m. its action is likely to last for roughly three hours. By that time the anopheles mosquito is most active in its biting activity and it can bite the person when he is sound asleep unless he gets up and applies the cream again. It may be remembered that anopheles comes quietly and causes hardly any inconvenience to the person even immediately after the bite.

The best protection from mosquito bite at night is the use of proper mosquito net.

Problems in Malaria Control

At present there are two major problems in malaria control. They are (1) Resistance of malaria parasites to some of the potent anti malaria drugs and (2) Resistance of the malaria carrying mosquitoes to many of the available insecticides. Both these factors are the cause of current pessimistic outlook in malaria control.

Drug Resistance

Resistance of malaria parasites to an anti malarial drug is the ability of the particular parasite species

Such specifications have not yet been met although many substances have been tested. The fact that so many chemicals have been tried suggests all once that none of them proved satisfactory.

Certain new products have been developed which are much more useful than any of the older materials. Diethyltoluamide has been found to be an outstanding one. Others are Indalone, dimethyl phthalate, dimethyl carbate, ethyl hexamediol etc. They are fairly effective for upto a maximum of three to four hours.

The most commonly available material in India is dimethyl phthalate which is made up into cream.

Use of mosquito repellent cream is liable to give a false sense of protection. Applied at 9 or 10 p.m. its action is likely to last for roughly three hours. By that time the anopheles mosquito is most active in its biting activity and it can bite the person when he is sound asleep unless he gets up and applies the cream again. It may be remembered that anopheles comes quietly and causes hardly any inconvenience to the person even immediately after the bite.

The best protection from mosquito bite at night is the use of proper mosquito net.

Problems in Malaria Control

At present there are two major problems in malaria control. They are (1) Resistance of malaria parasites to some of the potent anti-malaria drugs and (2) Resistance of the malaria-carrying mosquitoes to many of the available insecticides. Both these factors are the cause of current pessimistic outlook in malaria control.

Drug Resistance

Resistance of malaria parasites to anti-malarial drug is the ability of the particular parasite species

Hippocrates and some other Greek and Roman scholars associated malaria with marshy areas and said that it was caused by the bad air arising from the stagnant water in the marshes. Later a Roman named Palladius, confirmed that the draining away of the marshes reduced the incidence of malarial fevers. He had even suggested that the disease might be caused by drinking water containing mosquito larvae.

Early in the nineteenth century when medical scientists examined under the microscope blood from patients suffering from malaria they noticed the presence of a large number of minute black specks. In 1878 Alphonse Laveran a French doctor serving with the army in Algeria noted that occasionally in the red blood cells of malaria patients there was a tiny pulsating colourless blob around whose edges the black specks emerged.

These observations of Laveran were useful in that they indicated an association between these organisms and malaria. But how did this organism get into the patient's blood was not known at all. Examination of the stagnant water from the ponds and ditches revealed no sign of it.

During the last quarter of the nineteenth century, there were scores of scientists in various countries, working on the problem of malaria transmission. Ronald Ross working in India succeeded in unveil

ing this mystery The story of his researches is very interesting indeed

Ross started work on the study of malaria in 1890, but till 1897 he had no success Meanwhile, he worked with and consulted top ranking parasitologists of the world

In 1897, after his return from England Ross set to work at Secunderabad He detected malaria organisms in some patients admitted in the hospital He surrounded these patients with nets and released mosquitoes within After the mosquitoes had drawn blood he captured and dissected them with a view to discovering the parasites within He frantically laboured at this job in the summer heat of Secunderabad Examination of each of the mosquitoes took him two three hours of intense peering through the microscope Of this stage of his researches he wrote The screws of microscope were rusted with sweat from my forehead and hands and its last remaining eye piece was cracked Search for the parasite inside the body of the mosquito was a tedious and time consuming task Ross wrote that under a microscope a mosquito appears as big as hippopotamus is to the naked eye and the object I am looking for need not necessarily be longer than say a nut or an apple and moreover he had no idea at all as to the position the parasite would take up in the enormous mass of cells of which

mosquito is composed

On 20th August 1897 while Ross was tired and his eyes were hurting he decided to look at the last but one specimen. He took the stomach out and searched the remainder of the body and again found nothing. He could scarcely bring himself to look at the numerous cells of the stomach tissue which under the microscope looked like a collection of flagstones. He had done it a thousand times before without any convincing result. He wrote: But the Angel of Fate fortunately laid his hand on my head. He saw a circular object which could not be one of the cells of the stomach tissue of the mosquito. In it were black granules exactly like those seen in the malarial blood. It at once dawned upon him that the organisms associated with malaria had gone into the walls of the mosquito's stomach. He laughed and shouted for his assistant but he had gone for his siesta. No No Ross cried to himself

Dame Nature you are a sorceress but you do not trick me so easily

The same day Ross wrote the following poem

This day designing God
Hath put into my hand
A wonderful thing And God
Be praised At this command
I have found thy secret deeds

Oh million murdering Death
I know that this little thing
A million men will save
On Death where is thy sting?
Thy victory Oh grave

In 1898 Ross confirmed and furthered his researches of malaria

Ross achieved success in spite of all the difficulties and hurdles put in his way. Nearly all of his medical colleagues in India regarded him as a crank, flying in the face of thousands of years of authority which laid down that malaria was due to bad air from marshes. They regarded his passion for mosquitoes as a crazy idea. His officers also thought likewise so much so that he was usually the last to be promoted and was always on the lowest rung of the salary scale. His requests for special leave to pursue his research were rejected while a colleague was granted six months leave for training of race horses!

At long last the value of his researches was recognized. In 1902 Ross was awarded the Nobel Prize for Medicine for his researches on malaria.

The researches on malaria after the work of Ross were mainly directed to finding out ways and means of controlling malaria.

In 1908 a devastating epidemic of malaria occurred in the Punjab and Uttar Pradesh which caused 307,316 deaths in two months. In 1910 the Central Malaria Bureau was founded which was later designed

14

What Can You Do To Prevent Malaria

Without the cooperation of all of us the malaria problem cannot be solved : Whatever the Government may do if cooperation of the people is not available *malaria will continue to menace us*

The following are the important precautions for all of us to observe in order to minimize the incidence of malaria around us

1 Eliminate breeding places of mosquitoes

See that air cooler and its water tank has no water in it when the cooler is not in use

The water tank of the air conditioner should not contain any water when it is not being used

Water in the flower vases kept inside the house be changed at least once a week

Discarded tins and other household materials kept on roof top or in any other open place where rain water can collect in them must be properly disposed of

Choked up drains near the houses may be reported to the municipal authorities to be cleaned

~~Fill~~ Fill either individually or collectively or insist upon the municipal authorities to fill pits burrows or ponds near your house

Ask the municipal health officer to arrange for oiling over the stagnant water which cannot be removed immediately

2 Destroy the Mosquito

Use flit or other similar sprays in your houses if mosquitoes are around

Request the municipal health officer to arrange to do pyrethrum spraying inside your house

3 Protect yourself from mosquito bite

Use mosquito nets at night if you live in an area where there are mosquitoes and malaria also occurs

4 Visit Malaria Clinic when necessary

Inform or visit malaria clinic nearest to house in case there is a case of fever. There are present over one hundred Malaria Clinics in working within the precincts of different or outside. Similar clinics are available in cities as well. These clinics provide both diagnosis and treatment facilities free. Cases reported also help in assessing whether malaria is increasing or decreasing in an area and whether the control measures being taken are effective or not.

5 Get treated promptly

By getting treated promptly when you have malaria, you not only protect yourself from its effects but protect others also in the process. When you take prompt treatment you not only kill the development of malaria parasites in your body which caused the fever but also those which infect a mosquito—the gametocytes. Thus, you break the cycle of man mosquito man malaria.

6 Inform as many people as possible about the mentioned measures to control malaria

By Helping To Control Malaria You Not Only Protect Others But Also Help Yourself and Your Family

